

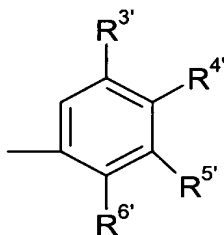
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1. A method of treating a disease, other than cancer, mediated by p-38, comprising administering a compound of formula I



or a pharmaceutically acceptable salt of a compound of formula I
wherein

A is



and

B is a substituted or unsubstituted, up to bicyclic aryl or heteroaryl moiety of up to 12 carbon atoms with at least one aromatic structure containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur, wherein if B is substituted, it is substituted by one or more substituents selected from the group consisting of halogen, up to per-halo, and W_n, wherein n is 0-3 and each W is independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)NR⁷R^{7'}, -C(O)-R⁷, -NO₂, -OR⁷, -SR⁷, -NR⁷R^{7'},

-NR⁷C(O)OR^{7'}, -NR⁷C(O)R^{7'}, C₁-C₁₀ alkyl, C₂₋₁₀-alkenyl, C₁₋₁₀-alkoxy, C₁₋₁₀ alkenoyl, C₃₋₁₀ cycloalkyl,

C₆₋₁₂ aryl, optionally substituted by halogen, C₁-C₁₀ alkyl or C₁₋₁₀-alkoxy,

C₇₋₂₄ alkaryl, C₃₋₁₃ heteroaryl, optionally substituted by halogen, C₁-C₁₀ alkyl or C₁₋₁₀-alkoxy,

substituted C₁-C₁₀ alkyl, substituted C₂₋₁₀-alkenyl, substituted C₁₋₁₀-alkoxy, substituted C₁₋₁₀ alkenoyl, substituted C₃₋₁₀ cycloalkyl, substituted C₄₋₂₃ alkheteroaryl optionally substituted by halogen, C₁-C₁₀ alkyl or C₁₋₁₀ alkoxy and M-L¹;

wherein if W is a substituted group which does not contain aryl or hetaryl, it is substituted by one or more substituents independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)R⁷, -C(O)NR⁷R^{7'}, -NO₂, -NR⁷C(O)OR^{7'}, -OR⁷, -SR⁷, -NR⁷R^{7'}, -NR⁷C(O)R^{7'}, and halogen up to per-halo;

wherein if B contains a phenyl group, W is additionally selected from the group consisting of hydroxy, OR^{1a}CONHR⁷, N(SO₂R⁷)₂, SO₂F, SOR⁷, SO₂R⁷, SO₂CH_pX^a_{3-p}, wherein p is 0-3, C₁₋₁₀ alkoxy substituted C₆₋₁₂ aryl, C₁₋₁₀ alkyl substituted C₆₋₁₂ aryl, halogen substituted C₆₋₁₂ aryl, C₁₋₁₀ alkyl substituted C₃₋₁₃ heteroaryl, C₁₋₁₀ alkoxy substituted C₃₋₁₃ hetaryl and halogen substituted C₃₋₁₃ hetaryl;

wherein each R⁷ and R^{7'} is independently selected from H, C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl, C₃₋₁₀ cycloalkyl, C₆₋₁₄ aryl, C₃₋₁₃ hetaryl, C₇₋₂₄ alkaryl, C₄₋₂₃ alkheteroaryl, up to per-halosubstituted C₁₋₁₀ alkyl, up to per-halosubstituted C₂₋₁₀-alkenyl, up to per-halosubstituted C₃₋₁₀ cycloalkyl, up to per-halosubstituted C₆₋₁₄ aryl and up to per-halosubstituted C₃₋₁₃ hetaryl;

R^{1a} is C₁₋₁₀ alkyl;

M is -O-, -S-, -N(R⁷)-, -(CH₂)_m-, -C(O)-, -CH(OH)-, -(CH₂)_mO-, -NR⁷C(O)NR⁷R^{7'}-, -NR⁷C(O)-, -C(O)NR⁷-, -(CH₂)_mS-, -(CH₂)_mN(R⁷)-, -O(CH₂)_m-, -CHX^a, -CX^a₂-, -S-(CH₂)_m- or -N(R⁷)(CH₂)_m-;

m = 1-3, and X^a is halogen; and

L¹ is a 5-10 member aromatic structure containing 0-2 members of the group consisting of nitrogen, oxygen and sulfur, wherein the aromatic structure is unsubstituted or substituted by halogen up to per-halo and optionally substituted by Z_{n1},

wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of -CN, -NO₂, -OR⁷, -SR⁷, -NR⁷R^{7'}, -NR⁷C(O)OR^{7'}, -NR⁷C(O)R^{7'}, C₁₋₁₀ alkyl, C₁₋₁₀ alkoxy, C₃₋₁₀ cycloalkyl, C₆₋₁₄ aryl, C₃₋₁₃ hetaryl, C₇₋₂₄ alkaryl, C₄₋₂₃ alkheteroaryl, substituted C₁₋₁₀ alkyl, substituted C₃₋₁₀ cycloalkyl, substituted C₇₋₂₄ alkaryl and substituted C₄₋₂₃ alkheteroaryl; wherein one or more substituents of Z is selected from the group consisting of -CN, -NO₂, -OR⁷, -SR⁷, -NR⁷R^{7'}, -NR⁷C(O)R^{7'}, and -NR⁷C(O)OR^{7'};

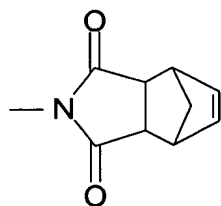
wherein R^{3'}, R^{4'}, R^{5'} and R^{6'} are each independently H, halogen, C₁₋₁₀ alkyl optionally substituted by halogen up to perhalo, C₁₋₁₀-alkoxy optionally substituted by at least one hydroxy group, C₁₋₁₀ alkoxy substituted by halogen up to perhaloalkoxy, C₆₋₁₂ aryl optionally substituted by C₁₋₁₀ alkoxy or halogen, C₅₋₁₂ hetaryl optionally substituted by C₁₋₁₀ alkyl, C₁₋₁₀ alkoxy, halogen, NO₂,

SO₂F, -SO₂CH_pX^a_{3-p}, -COOR¹, -OR^{1a}CONHR¹, -NHCOR¹, -NR^{1a}COR¹, -SR¹, NH₂, or -N(SO₂R¹)₂, and

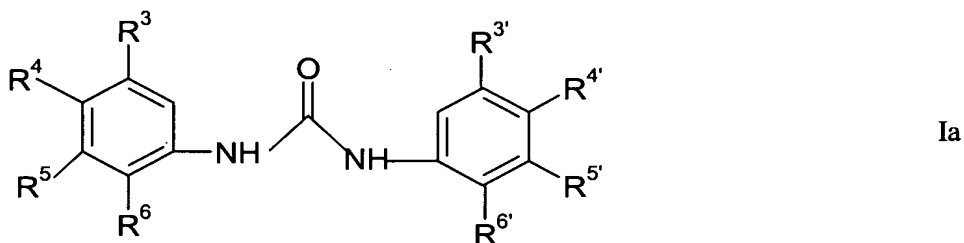
wherein 2 adjacent R^{3'}, R^{4'}, R^{5'} and R^{6'} can together with the phenyl form naphthyl, optionally substituted by C₁₋₁₀ alkyl, C₁₋₁₀ alkoxy, C₃₋₁₀-cycloalkyl, C₂₋₁₀-alkenyl, C₁₋₁₀-alkanoyl, and halogen up to perhalo;

wherein each R¹ is independently H or C₁₋₁₀ alkyl optionally substituted by halogen up to perhalo, R^{1a} is a C₁-C₁₀ alkyl, and R² is C₁₋₁₀-alkyl optionally substituted by halogen up to perhalo;

where L¹ is phenyl, it is also optionally substituted, by

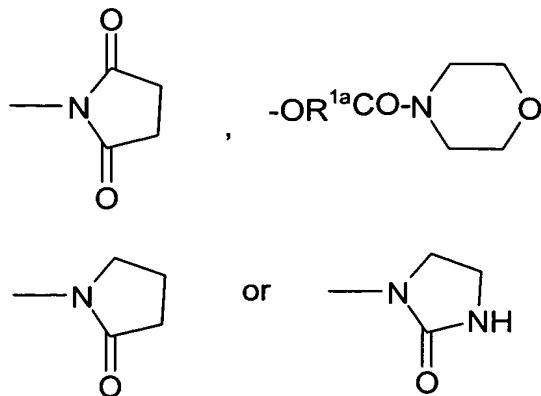


2. A method of treating a disease, other than cancer, mediated by p-38, comprising administering a compound of formula Ia



or a pharmaceutically acceptable salt thereof;

wherein R³, R⁴, R⁵, and R⁶ are each independently H, hydroxy, halogen, C₁₋₁₀-alkyl optionally substituted by halogen up to perhalo, C₁₋₁₀-alkoxy optionally substituted by at least one hydroxy group, C₁₋₁₀ alkoxy substituted by halogen up to perhalo; C₆₋₁₂ aryl optionally substituted by C₁₋₁₀ alkoxy or halogen; C₅₋₁₂ hetaryl optionally substituted by C₁₋₁₀ alkyl, C₁₋₁₀ alkoxy or halogen; NO₂, SO₂F, -SO₂CH_pX^a_{3-p}, -COOR¹, -OR^{1a}CONHR¹, -NHCOR¹, -SR¹, NH₂, -N(SO₂R¹)₂, furyloxy,



wherein X^a is halogen, each R¹ is independently H or C₁-C₁₀ alkyl optionally substituted by halogen up to per halo; R^{1a} is C₁-C₁₀ alkyl and p is 0-3 ; and

wherein 2 adjacent R³, R⁴, R⁵ and R⁶ can together form an aryl or hetaryl ring with 5-12 atoms, optionally substituted by C₁₋₁₀-alkyl, C₁₋₁₀-alkoxy, C₃₋₁₀-cycloalkyl, C₂₋₁₀-alkenyl, C₁₋₁₀-alkanoyl, C₆₋₁₂-aryl, C₅₋₁₂-hetaryl, C₆₋₁₂-aralkyl, C₆₋₁₂-alkaryl, halogen; -NR¹R¹; -NO₂; -CF₃; -COOR¹, -NHCOR¹, -CN, -CONR¹R¹, -SO₂R², -SOR² and -SR² with -SO₂ optionally incorporated in the aryl or hetaryl ring;

wherein each R¹ is independently H or C₁₋₁₀-alkyl optionally substituted by halogen up to per halo and R² is C₁₋₁₀-alkyl optionally substituted by halogen up to perhalo;

and wherein one of R³, R⁴, R⁵ or R⁶ can be -ML¹, where M and L¹ are as defined below with the proviso that if R³ and R⁶ are both H, then one of R⁴ or R⁵ is not H, and

M is -O-, -S-, -N(R⁷)-, -(CH₂)_m-, -C(O)-, -CH(OH)-, -(CH₂)_mO-, -NR⁷C(O)NR⁷R⁷-, -NR⁷C(O)-, -C(O)NR⁷-, -(CH₂)_mS-, -(CH₂)_mN(R⁷)-, -O(CH₂)_m-, -CHX^a, -CX^a₂-, -S-(CH₂)_m- and -N(R⁷)(CH₂)_m;

m = 1-3, and X^a is halogen; and

L¹ is a 5-10 member aromatic structure containing 0-2 members of the group consisting of nitrogen, oxygen and sulfur, wherein the aromatic structure is unsubstituted or substituted by halogen up to per-halo and optionally substituted by Z_{n1},

wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of -CN, -NO₂, -OR⁷, -SR⁷, -NR⁷R⁷, -NR⁷C(O)OR⁷, -NR⁷C(O)R⁷, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, C₃-C₁₀ cycloalkyl, C₆-C₁₂ aryl, C₃-C₁₃ hetaryl, C₇-C₂₄ alkaryl, C₄-C₂₃ alkheteroaryl, substituted C₁-C₁₀ alkyl, substituted C₃-C₁₀ cycloalkyl, substituted C₇-C₂₄ alkaryl and substituted C₄-C₂₃ alkheteroaryl;

wherein the one or more substituents of Z is selected from the group consisting of -CN, -NO₂, -OR⁷, -SR⁷, -NR⁷R^{7'}, -NR⁷C(O)R^{7'} and -NR⁷C(O)OR^{7'};

wherein R^{3'}, R^{4'}, R^{5'} and R^{6'} are each independently H, halogen, C₁₋₁₀ alkyl optionally substituted by halogen up to perhalo, C₁₋₁₀-alkoxy optionally substituted by at least one hydroxy group, C₁₋₁₀ alkoxy substituted by halogen up to perhaloalkoxy, C₆₋₁₂ aryl optionally substituted by C₁₋₁₀ alkoxy or halogen, C₅₋₁₂ hetaryl optionally substituted by C₁₋₁₀ alkyl, C₁₋₁₀ alkoxy or halogen, NO₂, SO₂F, -SO₂CH_pX^a_{3-p}, -COOR¹, -OR^{1a}CONHR¹, -NHCOR¹, -NR^{1a}COR¹, -SR¹, NH₂, or -N(SO₂R¹)₂,

wherein each R¹ is independently H or C₁₋₁₀ alkyl optionally substituted by halogen up to perhalo, R^{1a} is C₁₋₁₀ alkyl, X^a is halogen, and p is 0 or 1, and

wherein 2 adjacent R^{3'}, R^{4'}, R^{5'} and R^{6'} can together with the phenyl form naphthyl, optionally substituted by C₁₋₁₀ alkyl, C₁₋₁₀ alkoxy, C₃₋₁₀-cycloalkyl, C₂₋₁₀-alkenyl, C₁₋₁₀-alkanoyl, and halogen up to perhalo.

3. A method according to claim 2, wherein

R^{3'} is H, halogen, C₁₋₁₀-alkyl optionally substituted by halogen, up to perhalo, NO₂, -SO₂F or -SO₂CF₃;

R^{4'} is H, halogen, C₁₋₁₀-alkyl, C₁₋₁₀-alkoxy, halogen or NO₂;

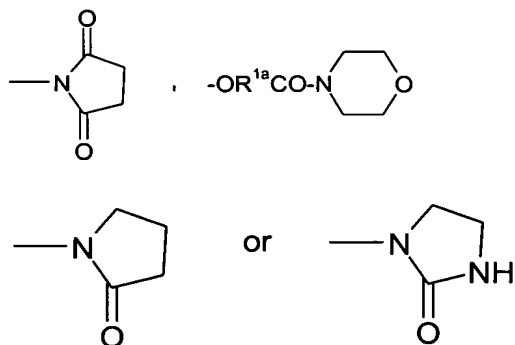
R^{5'} is H or C₁₋₁₀-alkyl optionally substituted by halogen, up to perhalo;

R^{6'} is H, C₁₋₁₀-alkoxy optionally substituted by at least one hydroxy group; -COOR¹; -OR^{1a}CONHR¹; -NHCOR¹; -SR¹; phenyl optionally substituted by halo or C₁₋₁₀-alkoxy; NH₂; or -N(SO₂R¹)₂.

4. A method according to claim 2, wherein

R³ is Cl, F, C₄₋₅-branched alkyl optionally substituted by halogen up to perhalo, -SO₂F or -SO₂CF₃; and

R⁶ is C₁₋₁₀-alkoxy optionally substituted by at least one hydroxy group, -COOR¹, -OR^{1a}CONHR¹, -NHCOR¹, -SR¹, phenyl optionally substituted by halo or C₁₋₁₀-alkoxy, NH₂, -N(SO₂R¹)₂, furyloxy,



5. A method according to claim 2, wherein R^{4'} is C₁₋₁₀-alkyl or halogen; R^{5'} is H, C₁₋₁₀-alkyl, halogen, CF₃, NO₂ or NH₂; and R^{6'} is H, C₁₋₁₀-alkyl, or halogen.

6. A method according to claim 2, wherein R^{5'} is C₁₋₁₀-alkyl, halogen, CF₃, halogen, NO₂ or NH₂.

7. A method according to claim 2, wherein R^{6'} is C₁₋₁₀-alkyl, halogen, -NHCOCH₃ or -N(CH₃)COCH₃.

8. A method according to claim 4, wherein R^{3'} is t-butyl or CF₃ and R^{6'} is OCH₃.

9. A method according to claim 2, wherein the disease is mediated by a cytokine or protease regulated by p38.

10. A method according to claim 2, wherein the disease is mediated by TNF α , MMP-1, MMP-3, IL-1, IL-6 or IL-8.

11. A method according to claim 2, wherein the disease is an inflammatory or immunomodulatory disease.

12. A method according to claim 2, wherein the disease is osteoarthritis, rheumatoid arthritis, osteoporosis, asthma, septic shock, or inflammatory bowel disease.

13. A method according to claim 39, wherein the compound of formula I is

N-(5-tert-Butyl-2-methoxyphenyl)-N¹-(4-phenyloxyphenyl)urea;

N-(5-tert-Butyl-2-methoxyphenyl)-N¹-(4-(4-methoxyphenoxy)phenyl)urea;

N-(5-tert-Butyl-2-methoxyphenyl)-N¹-(4-(4-pyridinyloxy)phenyl)urea;

N-(5-tert-Butyl-2-methoxyphenyl)-N¹-(4-(4-pyridinylmethyl)phenyl)urea;

N-(5-tert-Butyl-2-methoxyphenyl)-N¹-(4-(4-pyridinylthio)phenyl)urea;

N-(5-tert-Butyl-2-methoxyphenyl)-N¹-(4-(4-(4,7-methano-1H-isoindole-1,3(2H)-dionyl)methyl)phenyl)urea;

N-(5-tert-Butyl-2-phenylphenyl)-N¹-(2,3-dichlorophenyl)urea;

N-(5-tert-Butyl-2-(3-thienyl)phenyl)-N¹-(2,3-dichlorophenyl)urea;

N-(5-tert-Butyl-2-(N-methylaminocarbonyl)methoxyphenyl)-N¹-(2,3-dichlorophenyl)urea;

N-(5-tert-Butyl-2-(N-methylaminocarbonyl)methoxyphenyl)-N¹-(1-naphthyl)urea;

N-(5-tert-Butyl-2-(N-morpholinocarbonyl)methoxyphenyl)-N¹-(2,3-dichlorophenyl)urea;

N-(5-tert-Butyl-2-(N-morpholinocarbonyl)methoxyphenyl)-N¹-(1-naphthyl)urea;

N-(5-tert-Butyl-2-methoxyphenyl)-N¹-(4-(3-pyridinyl)methylphenyl)urea;

N-(5-tert-Butyl-2-(3-tetrahydrofuranyloxy)phenyl)-N¹-(2,3-dichlorophenyl)urea;

N-(5-Trifluoromethyl-2-methoxyphenyl)-N¹-(4-methylphenyl)urea;

N-(5-Trifluoromethyl-2-methoxyphenyl)-N¹-(4-methyl-2-fluorophenyl)urea;

N-(5-Trifluoromethyl-2-methoxyphenyl)-N¹-(4-fluoro-3-chlorophenyl)urea;

N-(5-Trifluoromethyl-2-methoxyphenyl)-N¹-(4-methyl-3-chlorophenyl)urea;

N-(5-Trifluoromethyl-2-methoxyphenyl)-N¹-(4-methyl-3-fluorophenyl)urea;

N-(5-Trifluoromethyl-2-methoxyphenyl)-N¹-(2,4-difluorophenyl)urea;

N-(5-Trifluoromethyl-2-methoxyphenyl)-N¹-(4-phenyloxy-3,5-dichlorophenyl)urea;

N-(5-Trifluoromethyl-2-methoxyphenyl)-N¹-(4-(4-pyridinylmethyl)phenyl)urea;

N-(5-Trifluoromethyl-2-methoxyphenyl)-N¹-(4-(4-pyridinylthio)phenyl)urea;

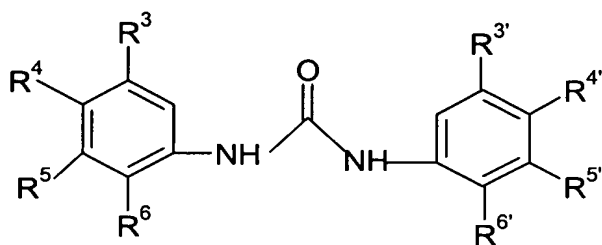
N-(5-Trifluoromethyl-2-methoxyphenyl)-N¹-(4-(4-pyridinyloxy)phenyl)urea;

N-(5-Trifluoromethyl-2-methoxyphenyl)-N¹-(3-(4-pyridinylthio)phenyl)urea;

N-(5-Trifluoromethyl-2-methoxyphenyl)-N¹-(4-(3-(N-methylaminocarbonyl)-phenyloxy)phenyl)-urea;

N-(5-Fluorosulfonyl)-2-methoxyphenyl)-N'-(4-methylphenyl)urea;
 N-(5-(Difluoromethanesulfonyl)-2-methoxyphenyl)-N'-(4-methylphenyl)urea;
 N-(5-(Difluoromethanesulfonyl)-2-methoxyphenyl)-N'-(4-fluorophenyl)urea;
 N-(5-(Difluoromethanesulfonyl)-2-methoxyphenyl)-N'-(4-methyl-2-fluorophenyl)urea;
 N-(5-(Difluoromethanesulfonyl)-2-methoxyphenyl)-N'-(4-methyl-3-fluorophenyl)urea;
 N-(5-(Difluoromethanesulfonyl)-2-methoxyphenyl)-N'-(4-methyl-3-chlorophenyl)urea;
 N-(5-(Difluoromethanesulfonyl)-2-methoxyphenyl)-N'-(4-fluoro-3-chlorophenyl)urea;
 N-(5-(Difluoromethanesulfonyl)-2-methoxyphenyl)-N'-(4-fluoro-3-methylphenyl)urea;
 N-(5-(Difluoromethanesulfonyl)-2-methoxyphenyl)-N'-(2,3-dimethylphenyl)urea;
 N-(5-(Trifluoromethanesulfonyl)-2-methoxyphenyl)-N'-(4-methylphenyl)urea;
 N-(3-methoxy-2-naphthyl)-N'-(2-fluorophenyl)urea;
 N-(3-Methoxy-2-naphthyl)-N'-(4-methylphenyl)urea;
 N-(3-Methoxy-2-naphthyl)-N'-(3-fluorophenyl)urea;
 N-(3-Methoxy-2-naphthyl)-N'-(4-methyl-3-fluorophenyl)urea;
 N-(3-Methoxy-2-naphthyl)-N'-(2,3-dimethylphenyl)urea;
 N-(3-Methoxy-2-naphthyl)-N'-(1-naphthyl)urea;
 N-(3-Methoxy-2-naphthyl)-N'-(4-(4-pyridinylmethyl)phenyl)urea;
 N-(3-Methoxy-2-naphthyl)-N'-(4-(4-pyridinylthio)phenyl)urea;
 N-(3-Methoxy-2-naphthyl)-N'-(4-(4-methoxyphenoxy)phenyl)urea; and
 N-(3-Methoxy-2-naphthyl)-N'-(4-(4-(4,7-methano-1H-isoindole-1,3(2H)-
 dionyl)methyl)phenyl)urea.
 N-(2-Hydroxy-4-nitro-5-chlorophenyl)-N'-(phenyl)urea; or
 N-(2-Hydroxy-4-nitro-5-chlorophenyl)-N'-(4-(4-pyridinylmethly)phenyl)urea.

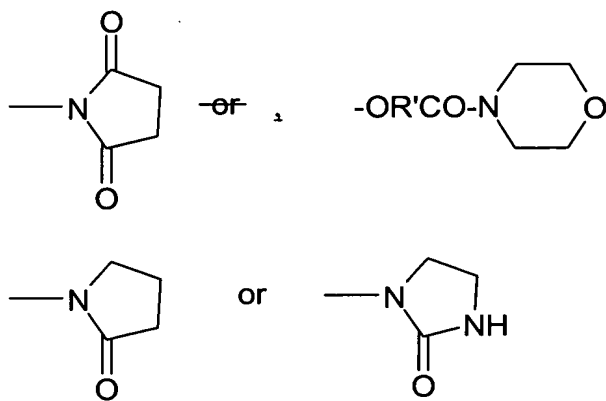
14. A compound of formula II



II

wherein

R^3 , R^4 , R^5 , and R^6 are each independently H; halogen; C_{1-10} -alkyl optionally substituted by halogen up to perhalo; C_{1-10} -alkoxy optionally substituted by at least one hydroxy group; NO_2 ; SO_2F ; $-SO_2CH_nX_{3-n}$; $-COOR^1$; $-OR^1CONHR^1$; $-NHCOR^1$; $-SR^1$; phenyl optionally substituted by halogen or C_{1-10} -alkoxy; NH_2 ; $-N(SO_2R^1)_2$; furyloxy;



2 adjacent R^3 - R^6 can together form an aryl or hetaryl ring with 5-12 atoms, optionally substituted by C_{1-10} -alkyl, C_{1-10} -alkoxy, C_{3-10} -cycloalkyl, C_{2-10} -alkenyl, C_{1-10} -alkanoyl, C_{6-12} -aryl, C_{5-12} -hetaryl, C_{6-12} -aralkyl, C_{6-12} -alkaryl, halogen; $-NR^1$; $-NO_2$; $-CF_3$; $-COOR^1$; $-NHCOR^1$; $-CN$; $-CONR^1R^1$; $-SO_2R^2$; $-SOR^2$; $-SR^2$; in which R^1 is H or C_{1-10} -alkyl and R^2 is C_{1-10} -alkyl;

R^3 , R^4 and R^5 are each independently H, C_{1-10} -alkyl, optionally substituted by halogen, up to perhalo; halogen; NO_2 or NH_2 ;

R^6 is H, C_{1-10} -alkyl, halogen, $-NHCOR^1$; $-NR^1COR^1$; NO_2 ;

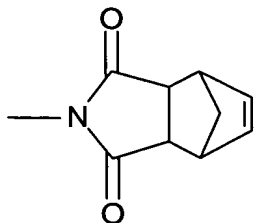
or 2 adjacent R^4 - R^6 can together be an aryl or hetaryl ring with 5-12 atoms;

R^1 is C_{1-10} -alkyl;

n is 0 or 1;

X is $-CH_2-$, $-S-$ or $-O-$; and

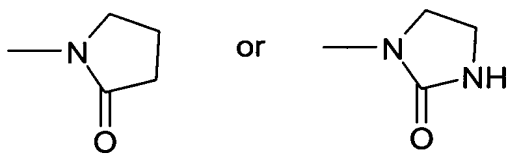
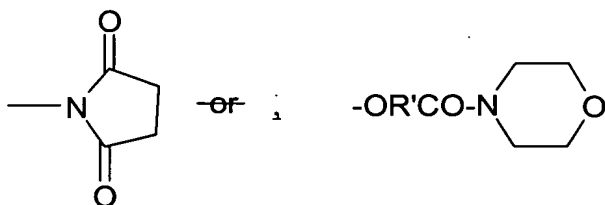
Y is phenyl, pyridyl, naphthyl or benzothiazole, each optionally substituted by C_{1-10} -alkyl, C_{1-10} -alkoxy, halogen or NO_2 or, where Y is phenyl, by



or a pharmaceutically acceptable salt thereof,

with the provisos that

- (a) if R^3 and R^6 are both H, one of R^4 or R^5 is not H,
- (b) R^6 is phenyl substituted by alkoxy or halogen, alkoxy substituted by hydroxy, $-\text{SO}_2\text{CF}_2\text{H}$, $-\text{OR}^1\text{CONHR}^1$, furyloxy, $\text{N}(\text{SO}_2\text{R}^1)_2$,



or R^3 is $\text{SO}_2\text{CF}_2\text{H}$, and

- (c) the compounds have a pKa greater than 10.

15.-16. (Canceled)

17. A compound according to claim 40, wherein $R^{4'}$ is C_{1-10} -alkyl or halogen; $R^{5'}$ is H, C_{1-10} -alkyl, halogen, CF_3 , halogen, NO_2 or NH_2 ; and $R^{6'}$ is H, C_{1-10} -alkyl, halogen, $-\text{NHCOCH}_3$, $-\text{N}(\text{CH}_3)\text{COCH}_3$, or NO_2 .

18. A compound according to claim 40, wherein $R^{3'}$ is t-butyl or CF_3 and $R^{6'}$ is $-\text{OCH}_3$.

19. A compound which is

N-(5-tert-Butyl-2-(N-methylaminocarbonyl)methoxyphenyl)-N'-(2,3-dichlorophenyl)urea;
N-(5-tert-Butyl-2-(N-methylaminocarbonyl)methoxyphenyl)-N'-(1-naphthyl)urea;
N-(5-tert-Butyl-2-(N-morpholinocarbonyl)methoxyphenyl)-N'-(2,3-dichlorophenyl)urea;
N-(5-tert-Butyl-2-(N-morpholinocarbonyl)methoxyphenyl)-N'-(1-naphthyl)urea;
N-(5-tert-Butyl-2-(3-tetrahydrofuranyloxy)phenyl)-N'-(2,3-dichlorophenyl)urea;
N-(5-(Difluoromethanesulfonyl)-2-methoxyphenyl)-N'-(4-methylphenyl)urea;
N-(5-(Difluoromethanesulfonyl)-2-methoxyphenyl)-N'-(4-fluorophenyl)urea;
N-(5-(Difluoromethanesulfonyl)-2-methoxyphenyl)-N'-(4-methyl-2-fluorophenyl)urea;
N-(5-(Difluoromethanesulfonyl)-2-methoxyphenyl)-N'-(4-methyl-3-fluorophenyl)urea;
N-(5-(Difluoromethanesulfonyl)-2-methoxyphenyl)-N'-(4-methyl-3-chlorophenyl)urea;
N-(5-(Difluoromethanesulfonyl)-2-methoxyphenyl)-N'-(4-fluoro-3-chlorophenyl)urea;
N-(5-(Difluoromethanesulfonyl)-2-methoxyphenyl)-N'-(4-fluoro-3-methylphenyl)urea;
N-(5-(Difluoromethanesulfonyl)-2-methoxyphenyl)-N'-(2,3-dimethylphenyl)urea; or
N-(5-(Trifluoromethanesulfonyl)-2-methoxyphenyl)-N'-(4-methylphenyl)urea.

20. (Canceled)

21. A pharmaceutical composition comprising a compound of claim 40, and a physiologically acceptable carrier.

22. A pharmaceutical composition comprising a compound of claim 43, and a physiologically acceptable carrier.

23. A method according to claim 2, wherein the disease is the result of host-versus-graft reactions.

24.-25. (Canceled)

26. A compound as in claim 44 wherein R^{3'} is hydrogen, halogen, C₁-C₁₀ alkyl substituted by halogen up to perhalo, C₁-C₁₀ alkoxy substituted by halogen up to perhalo, -NHCOR¹, -NR^{1a}COR¹, SO₂F, -NR^{1a}CONR¹, or -SO₂CH_pX^a_{3-p}.

27. A compound as in claim 44 wherein R^{3'} is hydrogen, Cl, F, C₄₋₅ branched alkyl, -SO₂F, -SO₂CF₃ or -CF₃,

28. (Canceled)

29. A compound as in claim 44 wherein R^{3'} is t-butyl, -CF₃, hydrogen, -SO₂CHF₂ or SO₂F.

30. (Canceled)

31. A compound as in claim 45 wherein R^{6'} is independently H; halogen; C₁₋₁₀- alkyl optionally substituted by halogen up to perhalo; C₁₋₁₀-alkoxy optionally substituted by at least one hydroxy group; NO₂; -SO₂CF₂H; -COOR¹; -OR^{1a}CONHR¹; -SR¹; -NH₂, -N(SO₂R¹)₂, -NR¹COR¹, furyloxy, morpholinocarbonyl, 2,5-dioxo-1-pyrrolindiy, thiophene or phenyl substituted by halogen or alkoxy.

32. A compound as in claim 45 wherein R^{6'} is phenyl substituted by halo or C₁₋₁₀ alkoxy, NH₂, -N(SO₂R¹)₂, furyloxy, thiophene, morpholinocarbonyl, 2,5-dioxo-1-pyrrolidiny, thiophene, -SR¹, COOR¹ or -OR^{1a}CONHR¹.

33. (Canceled)

34. A compound which is

N-(5-tert-Butyl-2-(N-methylaminocarbonyl)methoxyphenyl)-N'-(2,3-

dichlorophenyl)urea;

N-(5-tert-Butyl-2-(N-methylaminocarbonyl)methoxyphenyl)-N'-(1-naphthyl)urea;

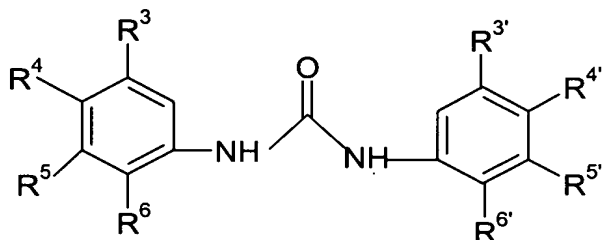
N-(5-tert-Butyl-2-(N-morpholinocarbonyl)methoxyphenyl)-N'-(2,3-dichlorophenyl)urea;

N-(5-tert-Butyl-2-(N-morpholinocarbonyl)methoxyphenyl)-N'-(1-naphthyl)urea;
 N-(5-tert-Butyl-2-(3-tetrahydrofuranyloxy)phenyl)-N'-(2,3-dichlorophenyl)urea;
 N-(5-(Difluoromethanesulfonyl)-2-methoxyphenyl)-N'-(4-methylphenyl)urea;
 N-(5-(Difluoromethanesulfonyl)-2-methoxyphenyl)-N'-(4-fluorophenyl)urea;
 N-(5-(Difluoromethanesulfonyl)-2-methoxyphenyl)-N'-(4-methyl-2-fluorophenyl)urea;
 N-(5-(Difluoromethanesulfonyl)-2-methoxyphenyl)-N'-(4-methyl-3-fluorophenyl)urea;
 N-(5-(Difluoromethanesulfonyl)-2-methoxyphenyl)-N'-(4-methyl-3-chlorophenyl)urea;
 N-(5-(Difluoromethanesulfonyl)-2-methoxyphenyl)-N'-(4-fluoro-3-chlorophenyl)urea;
 N-(5-(Difluoromethanesulfonyl)-2-methoxyphenyl)-N'-(4-fluoro-3-methylphenyl)urea;
 N-(5-(Difluoromethanesulfonyl)-2-methoxyphenyl)-N'-(2,3-dimethylphenyl)urea; or
 N-(5-(Trifluoromethanesulfonyl)-2-methoxyphenyl)-N'-(4-methylphenyl)urea.

35. A pharmaceutical composition comprising a compound of claim 44, and a physiologically acceptable carrier.

36. A pharmaceutical composition comprising a compound of claim 45, and a physiologically acceptable carrier.

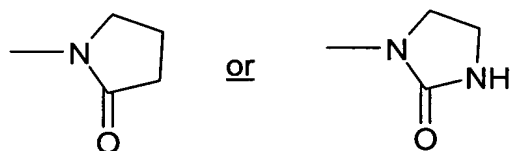
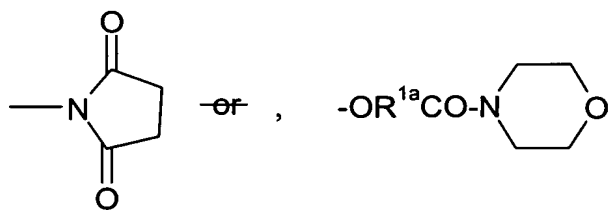
37. A compound of formula II



II

wherein

R³, R⁴, R⁵, and R⁶ are each independently H; halogen; C₁₋₁₀-alkyl optionally substituted by halogen up to perhalo; C₁₋₁₀-alkoxy optionally substituted by at least one hydroxy group; NO₂; SO₂F; -SO₂CH_nX_{3-n}; -COOR¹; -OR¹CONHR¹; -NHCOR¹; -SR¹; C₆₋₁₂ aryl, optionally substituted by C₁₋₁₀-alkyl, C₁₋₁₀ alkoxy or halogen, C₅₋₁₂ hetaryl, optionally substituted by C₁₋₁₀ alkyl, C₁₋₁₀ alkoxy or halogen; NH₂; -N(SO₂R¹)₂; furyloxy;



2 adjacent R^3 , R^4 , R^5 , or R^6 can together with the phenyl form naphthyl, optionally substituted by C_{1-10} -alkyl, C_{1-10} -alkoxy, C_{3-10} -cycloalkyl, C_{2-10} -alkenyl, C_{1-10} -alkanoyl, C_{6-12} -aryl, C_{5-12} -hetaryl, C_{6-12} -aralkyl, C_{6-12} -alkaryl, halogen; NR^1R^1 , NO_2 ; $-CF_3$; $-COOR^1$; $-NHCOR^1$; $-CN$; $-CONR^1R^1$; $-SO_2R^2$; $-SOR^2$; $-SR^2$; in which R^{1a} is C_{1-10} alkyl R^1 is H or C_{1-10} -alkyl and R^2 is C_{1-10} -alkyl;

and wherein one of R^3 , R^4 , R^5 , or R^6 can be $-ML^1$, wherein L^1 and M are as defined below, $R^{3'}$, $R^{4'}$ and $R^{5'}$ are each independently H, C_{1-10} -alkyl, optionally substituted by halogen, up to perhalo; halogen; NO_2 or NH_2 ;

$R^{6'}$ is H, C_{1-10} -alkyl, halogen, $-NHCOR^1$; $-NR^1COR^1$; NO_2 ;

or 2 adjacent $R^{4'}$ - $R^{6'}$ can together be an aryl or hetaryl ring with 5-12 atoms;

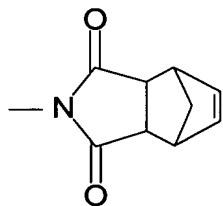
R^1 is C_{1-10} -alkyl;

n is 0 or 1;

M is $-CH_2-$, $-S-$, $N(CH_3)-$, $-NHC(O)-$, CH_2-S- , $-S-CH_2-$, $-C(O)-$, or $-O-$; and

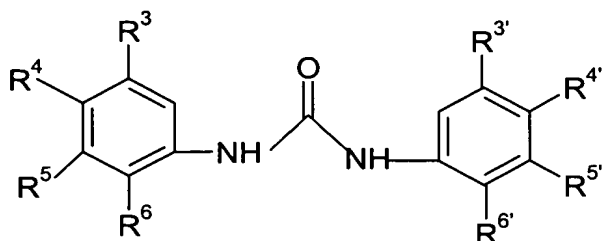
L^1 is phenyl, pyridyl, naphthyl, pyridone, pyrazine, benzodioxane, benzopyridine, pyrimidine or benzothiazole, each optionally substituted by

C_{1-10} -alkyl, C_{1-10} -alkoxy, halogen or NO_2 or, where L^1 is phenyl, by



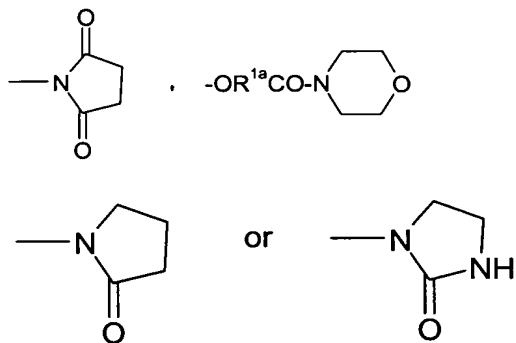
or a pharmaceutically acceptable salt thereof.

38. A compound of formula II



II

wherein R^3 , R^4 , R^5 , and R^6 are each independently H; halogen; C_{1-10} -alkyl optionally substituted by halogen up to perhalo; C_{1-10} -alkoxy optionally substituted by at least one hydroxy group; NO_2 ; SO_2F ; $-SO_2CH_nX_{3-n}$; $-COOR^1$; $-OR^1CONHR^1$; $-NHCOR^1$; $-SR^1$; phenyl optionally substituted by halogen or C_{1-10} -alkoxy; NH_2 ; $-N(SO_2R^1)_2$; furyloxy;



2 adjacent R^3 , R^4 , R^5 , and R^6 can together with phenyl form naphthyl, optionally substituted by C_{1-10} -alkyl, C_{1-10} -alkoxy, C_{3-10} -cycloalkyl, C_{2-10} -alkenyl, C_{1-10} -alkanoyl, C_{6-12} -aryl, C_{5-12} -hetaryl, C_{6-12} -aralkyl, C_{6-12} -alkaryl, halogen; $-NR^1$; $-NO_2$; $-CF_3$; $-COOR^1$; $-NHCOR^1$; $-CN$; $-CONR^1R^1$; $-SO_2R^2$; $-SOR^2$; $-SR^2$; in which R^1 is H or C_{1-10} -alkyl R^2 is C_{1-10} -alkyl; and R^{1a} is C_{1-10} alkyl.

a wherein one of R^3 , R^4 , R^5 , and R^6 can be ML^1 where M and L^1 are as defined below, $R^{3'}$, $R^{4'}$ and $R^{5'}$ are each independently H, C_{1-10} -alkyl, optionally substituted by halogen, up to perhalo; halogen; NO_2 or NH_2 ;

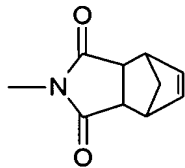
$R^{6'}$ is H, C_{1-10} -alkyl, halogen, $-NHCOR^1$; $-NR^1COR^1$; NO_2 ;

R^1 is C_{1-10} -alkyl;

n is 0 or 1;

M is $-CH_2-$, $-S-$ or $-O-$; and

L¹ is phenyl, pyridyl, naphthyl or benzothiazole, each optionally substituted by C₁₋₁₀-alkyl, C₁₋₁₀-alkoxy, halogen or NO₂ or, where L¹ is phenyl, by



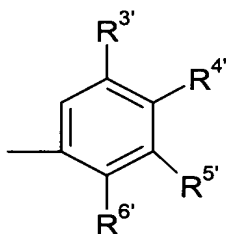
or a pharmaceutically acceptable salt thereof.

39. A method of treating a disease, other than cancer, mediated by p-38, comprising administering a compound of formula I



or a pharmaceutically acceptable salt of a compound of formula I wherein

A is



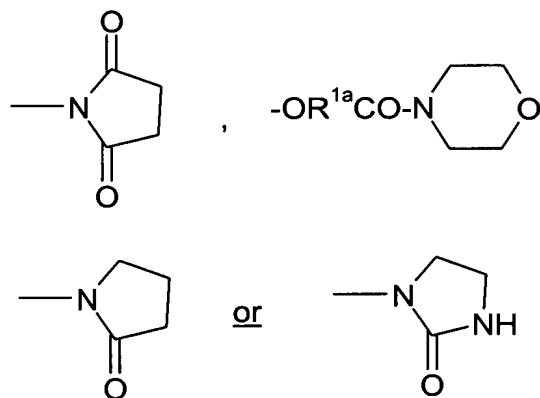
and

B is a substituted or unsubstituted, up to bicyclic aryl or heteroaryl moiety of up to 12 carbon atoms with at least one aromatic structure containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur, wherein if B is substituted, it is substituted by one or more substituents selected from the group consisting of halogen, up to per-halo, and W_n, wherein n is 0-3 and each W is independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)NR⁷R^{7'}, -C(O)-R⁷, -NO₂, -OR⁷, -SR⁷, -NR⁷R^{7'}, -NR⁷C(O)OR^{7'}, -NR⁷C(O)R^{7'}, C₁₋₁₀ alkyl, C₂₋₁₀-alkenyl, C₁₋₁₀-alkoxy, C₁₋₁₀ alkenoyl, C₃₋₁₀ cycloalkyl, C₆₋₁₂ aryl, optionally substituted by halogen, C₁₋₁₀ alkyl or C₁₋₁₀-alkoxy, C₇₋₂₄ alkaryl, C₃₋₁₃ heteroaryl, optionally substituted by halogen, C₁₋₁₀ alkyl or C₁₋₁₀-alkoxy; substituted

C₁-C₁₀ alkyl, substituted C₂₋₁₀-alkenyl, substituted C₁₋₁₀-alkoxy; substituted C₁₋₁₀ alkenoyl, halogen, substituted C₃-C₁₀ cycloalkyl, C₄-C₂₃ alketeroaryl optionally substituted by halogen, C₁-C₁₀ alkyl or C₁₋₁₀ alkoxy; and -M-L¹;

wherein if W is a substituted group which does not contain aryl or hetaryl, it is substituted by one or more substituents independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)R⁷, -C(O)NR⁷R^{7'}, -NO₂, -NR⁷C(O)OR^{7'}, -OR⁷, -SR⁷, -NR⁷R^{7'}, -NR⁷C(O)R^{7'}, and halogen up to per-halo;

wherein if B contains a phenyl group, W is additionally selected from the group consisting of hydroxy, OR^{1a}CONHR⁷, N(SO₂R⁷)₂, SO₂F, SOR⁷, SO₂R⁷, SO₂CH_pX^a_{3-p}, wherein p is 0-3, C₁₋₁₀ alkoxy substituted C₆-C₁₂ aryl, C₁-C₁₀ alky substituted C₆-C₁₂ aryl, halogen substituted C₆-C₁₂ aryl, C₁-C₁₀ alkyl substituted C₃-C₁₃ heteroaryl, C₁₋₁₀ alkoxy substituted C₃-C₁₃ hetaryl, halogen substituted C₃-C₁₃ hetaryl, furyloxy;



wherein each R⁷ and R^{7'} is independently selected from H, C₁-C₁₀ alkyl, C₂₋₁₀-alkenyl, C₃-C₁₀ cycloalkyl, C₆-C₁₄ aryl, C₃-C₁₃ hetaryl, C₇-C₂₄ alkaryl, C₄-C₂₃ alketeroaryl, up to per-halosubstituted C₁-C₁₀ alkyl, up to per-halosubstituted C₂₋₁₀-alkenyl, up to per-halosubstituted C₃-C₁₀ cycloalkyl, up to per-halosubstituted C₆-C₁₄ aryl and up to per-halosubstituted C₃-C₁₃ hetaryl;

R^{1a} is C₁-C₁₀ alkyl;

M is -O-, -S-, -N(R⁷)-, -(CH₂)_m-, -C(O)-, -CH(OH)-, -(CH₂)_mO-, -NR⁷C(O)NR⁷R^{7'}-, -NR⁷C(O)-, -C(O)NR⁷-, -(CH₂)_mS-, -(CH₂)_mN(R⁷)-, -O(CH₂)_m-, -CHX^a, -CX^a₂-, -S-(CH₂)_m- and -N(R⁷)(CH₂)_m-;

m = 1-3, and X^a is halogen; and

L^1 is a 5-10 member aromatic structure containing 0-2 members of the group consisting of nitrogen, oxygen and sulfur, wherein the aromatic structure is unsubstituted or substituted by halogen up to per-halo and optionally substituted by Z_{n1} ,

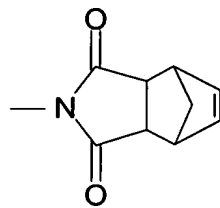
wherein $n1$ is 0 to 3 and each Z is independently selected from the group consisting of $-CN$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^7$, $-NR^7C(O)OR^7$, $-NR^7C(O)R^7$, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, C_3-C_{10} cycloalkyl, C_6-C_{12} aryl, C_3-C_{13} hetaryl, C_7-C_{24} alkaryl, C_4-C_{23} alkheteroaryl, substituted C_1-C_{10} alkyl, substituted C_3-C_{10} cycloalkyl, substituted C_7-C_{24} alkaryl and substituted C_4-C_{23} alkheteroaryl; wherein the one or more substituents of Z is selected from the group consisting of $-CN$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^7$, $-NR^7C(O)R^7$ and $-NR^7C(O)OR^7$;

wherein R^3 , R^4 , R^5 and R^6 are each independently H, halogen, C_{1-10} alkyl optionally substituted by halogen up to perhalo, C_{1-10} -alkoxy optionally substituted by at least one hydroxy group, C_{1-10} alkoxy substituted by halogen up to perhaloalkoxy, C_{6-12} aryl optionally substituted by C_{1-10} alkoxy or halogen, C_{5-12} hetaryl optionally substituted by C_{1-10} alkyl, C_{1-10} alkoxy or halogen, NO_2 , SO_2F , $-SO_2CH_pX^a_{3-p}$, $-COOR^1$, $-OR^{1a}CONHR^1$, $-NHCOR^1$, $-NR^{1a}COR^1$, $-SR^1$, NH_2 , or $-N(SO_2R^1)_2$,

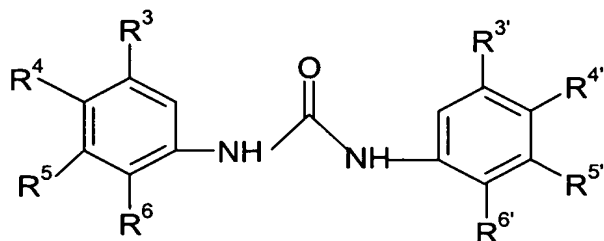
wherein each R^1 is independently H or C_{1-10} alkyl optionally substituted by halogen up to perhalo, R^{1a} is C_1-C_{10} alkyl, X^a is halogen, and p is 0 or 1, and

wherein 2 adjacent R^3 , R^4 , R^5 and R^6 can together with the phenyl form naphthyl, optionally substituted by C_{1-10} alkyl, C_{1-10} alkoxy, C_{3-10} -cycloalkyl, C_{2-10} -alkenyl, C_{1-10} -alkanoyl, and, halogen up to perhalo; and

where L^1 is phenyl, it is also optionally substituted, by

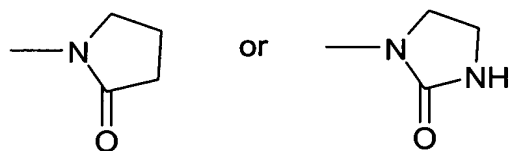
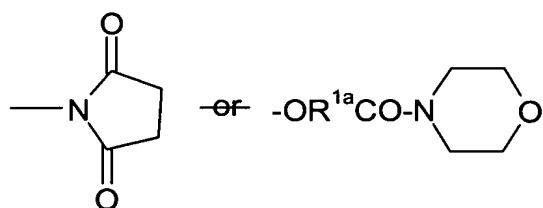


40. A compound of formula II



II

wherein R^3 , R^4 , R^5 , and R^6 are each independently H; halogen; C_{1-10} -alkyl optionally substituted by halogen up to perhalo; C_{1-10} -alkoxy optionally substituted by at least one hydroxy group; NO_2 ; SO_2F ; $-SO_2CH_nX^{a}_{3-n}$; $-COOR^1$; $-OR^{1a}CONHR^1$; $-NHCOR^1$; $-SR^1$; phenyl optionally substituted by halogen or C_{1-10} -alkoxy; NH_2 ; $-N(SO_2R^1)_2$; furyloxy;



wherein each R^1 is independently H or C_{1-10} alkyl optionally substituted by halogen up to perhalo, R^{1a} is C_1-C_{10} alkylene, X^a is halogen, and n is 0 or 1, and

wherein 2 adjacent R^3 , R^4 , R^5 and R^6 can together with the phenyl form an aryl or hetaryl ring with 5-12 atoms, optionally substituted by C_{1-10} -alkyl, C_{1-10} -alkoxy, C_{3-10} -cycloalkyl, C_{2-10} -alkenyl, C_{1-10} -alkanoyl, C_{6-12} -aryl, C_{5-12} -hetaryl, C_{6-12} -aralkyl, C_{6-12} -alkaryl, halogen; $-NR^1$; $-NO_2$; $-CF_3$; $-COOR^1$; $-NHCOR^1$; $-CN$; $-CONR^1R^1$; $-SO_2R^2$; $-SOR^2$; $-SR^2$; wherein each R^1 is independently H or C_{1-10} -alkyl and R^2 is C_{1-10} -alkyl;

and wherein one of R^3 , R^4 , R^5 or R^6 can be $-ML^1$, where L^1 and M are as defined below with the proviso that if R^3 and R^6 are both H, then one of R^4 or R^5 is not H, and

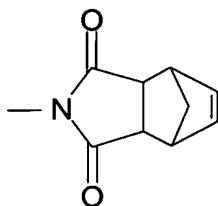
M is $-CH_2-$, $-S-$ or $-O-$; and

L^1 is phenyl, pyridyl, naphthyl or benzothiazole, each optionally substituted by C_{1-10} -alkyl, C_{1-10} -alkoxy, halogen or NO_2 ;

$R^{3'}$, $R^{4'}$ and $R^{5'}$ are each independently H, C_{1-10} -alkyl, optionally substituted by halogen, up to perhalo; halogen; NO_2 or NH_2 ;

$R^{6'}$ is H, C_{1-10} -alkyl, halogen, $-NHCOR^1$; $-NR^1COR^1$; NO_2 ; where R^1 is C_{1-10} -alkyl;

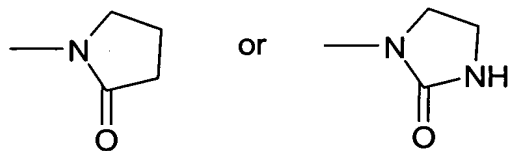
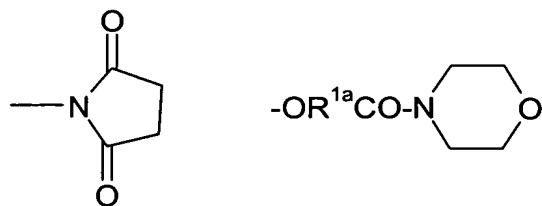
or wherein 2 adjacent $R^{3'}$, $R^{4'}$, $R^{5'}$ and $R^{6'}$ can together with the phenyl form naphthyl, optionally substituted by C_{1-10} alkyl, C_{1-10} alkoxy, C_{3-10} -cycloalkyl, C_{2-10} -alkenyl, C_{1-10} -alkanoyl, and, halogen up to perhalo; or where L^1 is phenyl, it is also optionally substituted, by



or a pharmaceutically acceptable salt thereof,

with the provisos that

(a) $R^{6'}$ is phenyl substituted by alkoxy, phenyl substituted by halogen, alkoxy substituted by hydroxy, $-SO_2CF_2H$, $-OR^1CONHR^1$, furyloxy, $-N(SO_2R^1)_2$;



or R^3 is SO_2CF_2H , and

(b) the compounds have a pK_a greater than 10.

41. A compound according to claim 40, wherein

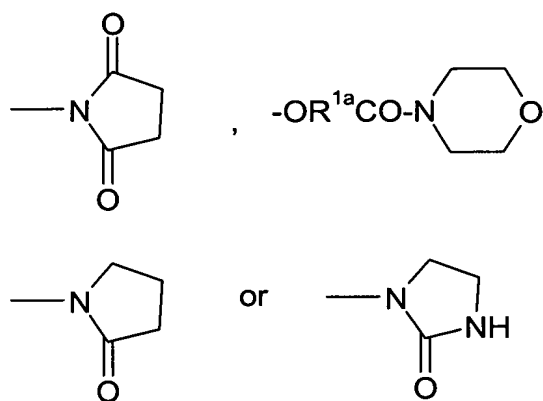
$R^{3'}$ is H, halogen or C_{1-10} -alkyl optionally substituted by halogen, up to perhalo, NO_2 , $-SO_2F$ or $-SO_2CF_3$;

$R^{4'}$ is H, C_{1-10} -alkyl, C_{1-10} -alkoxy, halogen or NO_2 ;

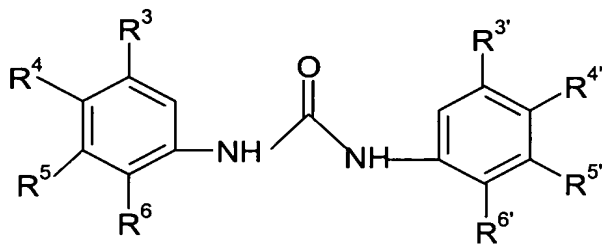
$R^{5'}$ is H or C_{1-10} -alkyl optionally substituted by halogen, up to perhalo;

R^6 is H or C_{1-10} -alkoxy optionally substituted by at least one hydroxy group; $-COOR^1$; $-OR^{1a}CONHR^1$; $-NHCOR^1$; $-SR^1$; phenyl optionally substituted by halo or C_{1-10} -alkoxy; NH_2 ; $-N(SO_2R^1)_2$.

42. A compound according to claim 40, wherein R^3 is Cl, F, C_{4-5} -branched alkyl, $-SO_2F$ or $-SO_2CF_3$; and R^6 is hydroxy; C_{1-10} -alkoxy optionally substituted by at least one hydroxy group; $-COOR^1$; $-OR^{1a}CONHR^1$; $-NHCOR^1$; $-SR^1$; phenyl optionally substituted by halo or C_{1-10} -alkoxy; NH_2 ; $-N(SO_2R^1)_2$, furyloxy,

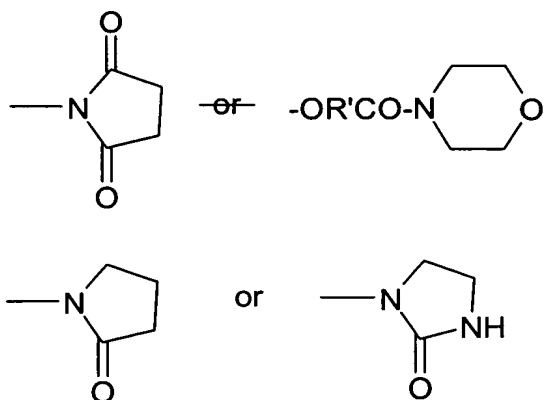


43. A compound of formula II



wherein

R^3 , R^4 , R^5 , and R^6 are each independently H; halogen; C_{1-10} -alkyl optionally substituted by halogen up to perhalo; C_{1-10} -alkoxy optionally substituted by at least one hydroxy group; NO_2 ; SO_2F ; $-SO_2CH_nX^{a}_{3-n}$; $-COOR^1$; $-OR^1CONHR^1$; $-NHCOR^1$; $-SR^1$; phenyl optionally substituted by halogen or C_{1-10} -alkoxy; NH_2 ; $-N(SO_2R^1)_2$; furyloxy;



wherein R^{1a} is C_{1-10} alkyl, n is 0 or 1, X^a is halogen, each R^1 is independently H or C_{1-10} or alkyl,

and wherein one of R^3 , R^4 , R^5 or R^6 can be $-ML^1$, where M and L^1 are as defined below with the proviso that if R^3 and R^6 are both H, then one of R^4 or R^5 is not H, and

M is $-CH_2-$, $-S-$ or $-O-$; and

L^1 is phenyl, pyridyl, naphthyl or benzothiazole, each optionally substituted by C_{1-10} -alkyl, C_{1-10} -alkoxy, halogen or NO_2 ;

2 adjacent R^3 , R^4 , R^5 and R^6 can together with the phenyl form naphthyl, optionally substituted by C_{1-10} -alkyl, C_{1-10} -alkoxy, C_{3-10} -cycloalkyl, C_{2-10} -alkenyl, C_{1-10} -alkanoyl, C_{6-12} -aryl, C_{5-12} -hetaryl, C_{6-12} -aralkyl, C_{6-12} -alkaryl, halogen; $-NR^1$; $-NO_2$; $-CF_3$; $-COOR^1$; $-NHCOR^1$; $-CN$; $-CONR^1R^1$; $-SO_2R^2$; $-SOR^2$; $-SR^2$; in which R^1 is H or C_{1-10} -alkyl, and R^2 is C_{1-10} -alkyl;

R^3 , R^4 and R^5 are each independently H, C_{1-10} -alkyl, optionally substituted by halogen, up to perhalo; halogen; NO_2 or NH_2 ;

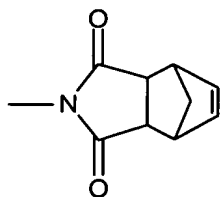
R^6 is H, C_{1-10} -alkyl, halogen, $-NHCOR^1$; $-NR^1COR^1$; NO_2 ;

or 2 adjacent R^4 - R^6 can together be an aryl or hetaryl ring with 5-12 atoms;

R^1 is C_{1-10} -alkyl;

n is 0 or 1;

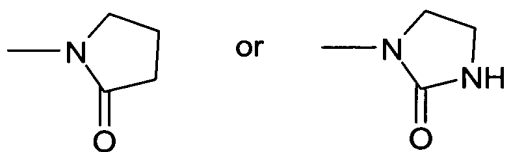
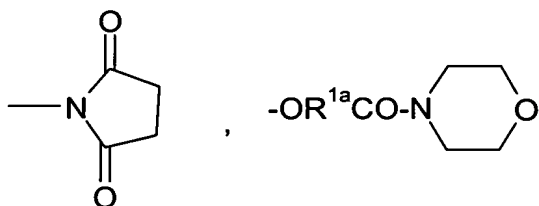
or, where L^1 is phenyl, by



or a pharmaceutically acceptable salt thereof

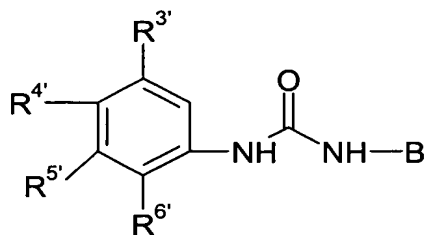
with the proviso that

(a) R^6 is alkoxy substituted by hydroxy, $-\text{SO}_2\text{CF}_2\text{H}$, $-\text{OR}^1\text{CONHR}^1$, furyloxy or $-\text{N}(\text{SO}_2\text{R}^1)_2$; or



or R^3 is $\text{SO}_2\text{CF}_2\text{H}$.

44. A compound of the formula



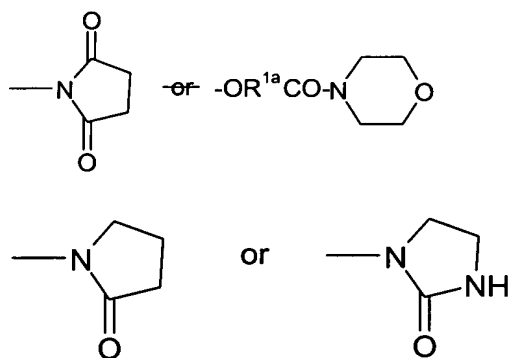
or a pharmaceutically acceptable salt thereof,

B is a substituted or unsubstituted, up to bicyclic aryl or heteroaryl moiety of up to 12 carbon atoms with at least one aromatic structure containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur, wherein if B is substituted, it is substituted by one or more substituents selected from the group consisting of halogen, up to per-halo, and W_n , wherein n is 0-3 and each W

is independently selected from the group consisting of $-\text{CN}$, $-\text{CO}_2\text{R}^7$, $-\text{C}(\text{O})\text{NR}^7\text{R}'$, $-\text{C}(\text{O})-\text{R}^7$, $-\text{NO}_2$, $-\text{OR}^7$, $-\text{SR}^7$, $-\text{NR}^7\text{R}'$, $-\text{NR}^7\text{C}(\text{O})\text{OR}^7$, $-\text{NR}^7\text{C}(\text{O})\text{R}'$, $\text{C}_1\text{-C}_{10}$ alkyl, C_{2-10} -alkenyl, C_{1-10} -alkoxy, $\text{C}_3\text{-C}_{10}$ cycloalkyl, $\text{C}_6\text{-C}_{14}$ aryl, optionally substituted by halogen, $\text{C}_7\text{-C}_{24}$ alkaryl, $\text{C}_3\text{-C}_{13}$ heteroaryl, optionally substituted by halogen, $\text{C}_1\text{-C}_{10}$ alkyl or C_{1-10} -alkoxy, $\text{C}_4\text{-C}_{23}$ alkheteroaryl, substituted $\text{C}_1\text{-C}_{10}$ alkyl, substituted C_{2-10} -alkenyl, substituted C_{1-10} -alkoxy, halogen, C_{1-10} -alkyl, C_{1-10} -alkoxy or halogen, substituted $\text{C}_3\text{-C}_{10}$ cycloalkyl, substituted $\text{C}_4\text{-C}_{23}$ alkheteroaryl and $-\text{ML}^1$;

wherein if W is a substituted group which does not contain aryl or heteroaryl, it is substituted by one or more substituents independently selected from the group consisting of $-\text{CN}$, $-\text{CO}_2\text{R}^7$, $-\text{C}(\text{O})\text{R}^7$, $-\text{C}(\text{O})\text{NR}^7\text{R}'$, $-\text{NO}_2$, $-\text{NR}^7\text{C}(\text{O})\text{OR}^7$, $-\text{OR}^7$, $-\text{SR}^7$, $-\text{NR}^7\text{R}'$, $-\text{NR}^7\text{C}(\text{O})\text{R}'$, and halogen up to per-halo;

wherein if B contains a phenyl group, W is additionally selected from the group consisting of hydroxy, $\text{OR}^{1a}\text{CONHR}^7$, $\text{N}(\text{SO}_2\text{R}^7)_2$, SO_2F , SOR^7 , SO_2R^7 , $\text{SO}_2\text{CH}_p\text{X}^a_{3-p}$, wherein p is 0-3, C_{1-10} alkoxy substituted $\text{C}_6\text{-C}_{12}$ aryl, $\text{C}_1\text{-C}_{10}$ alky substituted $\text{C}_6\text{-C}_{12}$ aryl, halogen substituted $\text{C}_6\text{-C}_{12}$ aryl, $\text{C}_1\text{-C}_{10}$ alkyl substituted $\text{C}_3\text{-C}_{13}$ heteroaryl, C_{1-10} alkoxy substituted $\text{C}_3\text{-C}_{13}$ heteroaryl, halogen substituted $\text{C}_3\text{-C}_{13}$ heteroaryl, furyloxy;



wherein each R^7 and R' are independently selected from H, $\text{C}_1\text{-C}_{10}$ alkyl, C_{2-10} -alkenyl, $\text{C}_3\text{-C}_{10}$ cycloalkyl, $\text{C}_6\text{-C}_{14}$ aryl, $\text{C}_3\text{-C}_{13}$ heteroaryl, $\text{C}_7\text{-C}_{24}$ alkaryl, $\text{C}_4\text{-C}_{23}$ alkheteroaryl, up to per-halosubstituted $\text{C}_1\text{-C}_{10}$ alkyl, up to per-halosubstituted C_{2-10} -alkenyl, up to per-halosubstituted $\text{C}_3\text{-C}_{10}$ cycloalkyl, up to per-halosubstituted $\text{C}_6\text{-C}_{14}$ aryl and up to per-halosubstituted $\text{C}_3\text{-C}_{13}$ heteroaryl,

R^{1a} is $\text{C}_1\text{-C}_{10}$ alkyl;

M is $-\text{O}-$, $-\text{S}-$, $-\text{N}(\text{R}^7)-$, $-(\text{CH}_2)_m-$, $-\text{C}(\text{O})-$, $-\text{CH}(\text{OH})-$, $-(\text{CH}_2)_m\text{O}-$, $-\text{NR}^7\text{C}(\text{O})\text{NR}^7\text{R}'$, $-\text{NR}^7\text{C}(\text{O})-$, $-\text{C}(\text{O})\text{NR}^7-$, $-(\text{CH}_2)_m\text{S}-$, $-(\text{CH}_2)_m\text{N}(\text{R}^7)-$, $-\text{O}(\text{CH}_2)_m-$, $-\text{CHX}^a$, $-\text{CX}^a_2-$, $-\text{S}(\text{CH}_2)_m-$ and $-\text{N}(\text{R}^7)(\text{CH}_2)_m-$;

m = 1-3, and X^a is halogen; and

L¹ is a 5-10 member aromatic structure containing 0-2 members of the group consisting of nitrogen, oxygen and sulfur, wherein the aromatic structure is unsubstituted or substituted by halogen up to per-halo and optionally substituted by Z_{n1},

wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of -CN, -NO₂, -OR⁷, -SR⁷, -NR⁷R^{7'}, -NR⁷C(O)OR^{7'}, -NR⁷C(O)R^{7'}, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, C₃-C₁₀ cycloalkyl, C₆-C₁₂ aryl, C₃-C₁₃ hetaryl, C₇-C₂₄ alkaryl, C₄-C₂₃ alkheteroaryl, substituted C₁-C₁₀ alkyl, substituted C₃-C₁₀ cycloalkyl, substituted C₇-C₂₄ alkaryl and substituted C₄-C₂₃ alkheteroaryl; wherein the one or more substituents of Z is selected from the group consisting of -CN, -NO₂, -OR⁷, -SR⁷, -NR⁷R^{7'}, -NR⁷C(O)R^{7'}, -NR⁷C(O)OR^{7'};

wherein R^{3'}, R^{4'} and R^{5'} are each independently H, hydroxy, halogen, C₁₋₁₀-alkyl optionally substituted by halogen up to perhalo, C₁₋₁₀-alkoxy optionally substituted by at least one hydroxy group, C₁-C₁₀ alkoxy substituted by or halogen up to perhalo, C₆₋₁₂ aryl optionally substituted by C₁₋₁₀ alkoxy or halogen, C₅₋₁₂ hetaryl optionally substituted by C₁₋₁₀ alkyl, C₁₋₁₀ alkoxy or halogen; NO₂, SO₂F, -SO₂CH_pX^a_{3-p}, -COOR¹, -OR^{1a}CONHR¹, -NHCOR¹, -NR^{1a}COR¹, -SR¹, NH₂, -N(SO₂R¹)₂, wherein

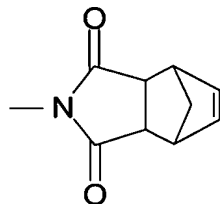
X^a is halogen, each R¹ is independently H or C₁-C₁₀ alkyl optionally substituted by halogen up to per halo;

R^{1a} is C₁-C₁₀ alkyl, and p is 0 or 1

and wherein

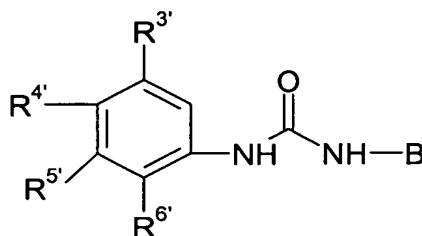
2 adjacent R^{3'}, R^{4'} and R^{5'} can together with the phenyl group form naphthyl, optionally substituted by C₁₋₁₀-alkyl, C₁₋₁₀-alkoxy, C₃₋₁₀-cycloalkyl, C₂₋₁₀-alkenyl, C₁₋₁₀-alkanoyl, and halogen up to per halo, and

where L¹ is phenyl, optionally by



wherein R^{6'} is -SO₂CF₂H, -COOR¹, -OR^{1a}CONHR¹, -SR¹, -NH₂, -N(SO₂R¹)₂, -NR¹COR¹, furyloxy, morpholinocarbonyl, 2,5-dioxo-1-pyrrolidinyl, thiophene, and phenyl substituted by halogen or alkoxy.

45. A compound of Formula II

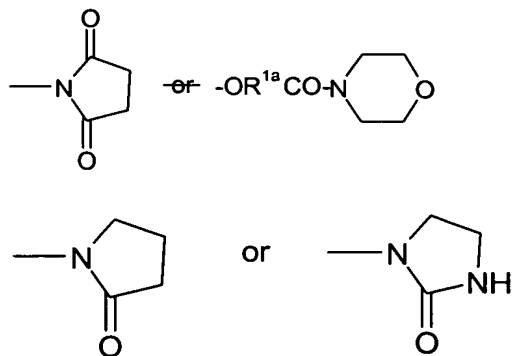


or a pharmaceutically acceptable salt thereof

B is a substituted or unsubstituted, up to bicyclic aryl or heteroaryl moiety of up to 12 carbon atoms with at least one aromatic structure containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur, wherein if B is substituted, it is substituted by one or more substituents selected from the group consisting of halogen, up to per-halo, and W_n, wherein n is 0-3 and each W is independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)NR⁷R^{7'}, -C(O)-R⁷, -NO₂, -OR⁷, -SR⁷, -NR⁷R^{7'}, -NR⁷C(O)OR^{7'}, -NR⁷C(O)R^{7'}, C₁-C₁₀ alkyl, C₂₋₁₀-alkenyl, C₁₋₁₀-alkoxy, C₃₋₁₀ cycloalkyl, C₆₋₁₄ aryl, optionally substituted by halogen, C₇₋₂₄ alkaryl, C₃₋₁₃ heteroaryl, optionally substituted by halogen, C₁₋₁₀ alkyl or C₁₋₁₀-alkoxy, C₄₋₂₃ alkheteroaryl, substituted C₁₋₁₀ alkyl, substituted C₂₋₁₀-alkenyl, substituted C₁₋₁₀-alkoxy, halogen, C₁₋₁₀-alkyl, C₁₋₁₀-alkoxy or halogen, substituted C₃₋₁₀ cycloalkyl, substituted C₄₋₂₃ alkheteroaryl and -ML¹;

wherein if W is a substituted group which does not contain aryl or hetaryl, it is substituted by one or more substituents independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)R⁷, -C(O)NR⁷R^{7'}, -NO₂, -NR⁷C(O)OR^{7'}, -OR⁷, -SR⁷, -NR⁷R^{7'}, -NR⁷C(O)R^{7'}, and halogen up to per-halo;

wherein if B contains a phenyl group, W is additionally selected from the group consisting of hydroxy, OR^{1a}CONHR⁷, N(SO₂R⁷)₂, SO₂F, SOR⁷, SO₂R⁷, SO₂CH_pX^a_{3-p}, wherein p is 0-3, C₁₋₁₀ alkoxy substituted C₆₋₁₂ aryl, C₁₋₁₀ alky substituted C₆₋₁₂ aryl, halogen substituted C₆₋₁₂ aryl, C₁₋₁₀ alkyl substituted C₃₋₁₃ heteroaryl, C₁₋₁₀ alkoxy substituted C₃₋₁₃ hetaryl, halogen substituted C₃₋₁₃ hetaryl, furyloxy;



wherein each R^7 and $R^{7'}$ are independently selected from H, C_1 - C_{10} alkyl, C_{2-10} -alkenyl, C_3 - C_{10} cycloalkyl, C_6 - C_{14} aryl, C_3 - C_{13} hetaryl, C_7 - C_{24} alkaryl, C_4 - C_{23} alkheteroaryl, up to per-halosubstituted C_1 - C_{10} alkyl, up to per-halosubstituted C_{2-10} -alkenyl, up to per-halosubstituted C_3 - C_{10} cycloalkyl, up to per-halosubstituted C_6 - C_{14} aryl and up to per-halosubstituted C_3 - C_{13} hetaryl,

R^{1a} is C_1 - C_{10} alkyl;

M is -O-, -S-, - $N(R^7)$ -, $-(CH_2)_m$ -, -C(O)-, -CH(OH)-, $-(CH_2)_mO$ -, $-NR^7C(O)NR^7R^{7'}$ -, $-NR^7C(O)$ -, -C(O) NR^7 -, $-(CH_2)_mS$ -, $-(CH_2)_mN(R^7)$ -, $-O(CH_2)_m$ -, $-CHX^a$ -, $-CX^a_2$ -, $-S(CH_2)_m$ - and $-N(R^7)(CH_2)_m$ -;

$m = 1-3$, and X^a is halogen; and

L^1 is a 5-10 member aromatic structure containing 0-2 members of the group consisting of nitrogen, oxygen and sulfur, wherein the aromatic structure is unsubstituted or substituted by halogen up to per-halo and optionally substituted by Z_{n1} ,

wherein $n1$ is 0 to 3 and each Z is independently selected from the group consisting of -CN, - NO_2 , - OR^7 , - SR^7 , - $NR^7R^{7'}$, - $NR^7C(O)OR^{7'}$, - $NR^7C(O)R^{7'}$, C_1 - C_{10} alkyl, C_1 - C_{10} alkoxy, C_3 - C_{10} cycloalkyl, C_6 - C_{12} aryl, C_3 - C_{13} hetaryl, C_7 - C_{24} alkaryl, C_4 - C_{23} alkheteroaryl, substituted C_1 - C_{10} alkyl, substituted C_3 - C_{10} cycloalkyl, substituted C_7 - C_{24} alkaryl and substituted C_4 - C_{23} alkheteroaryl; wherein the one or more substituents of Z is selected from the group consisting of -CN, - NO_2 , - OR^7 , - SR^7 , - $NR^7R^{7'}$, - $NR^7C(O)R^{7'}$, - $NR^7C(O)OR^{7'}$;

wherein $R^{4'}$, $R^{5'}$ and $R^{6'}$ are each independently H, hydroxy, halogen, C_{1-10} -alkyl optionally substituted by halogen up to perhalo, C_{1-10} -alkoxy optionally substituted by at least one hydroxy group, C_1 - C_{10} alkoxy substituted by or halogen up to perhalo, C_{6-12} aryl optionally substituted by C_1 -

₁₀ alkoxy or halogen, C₅₋₁₂ hetaryl optionally substituted by C₁₋₁₀ alkyl, C₁₋₁₀ alkoxy or halogen, NO₂, SO₂F, -SO₂CH_pX^a_{3-p}, -COOR¹, -OR^{1a}CONHR¹, -NHCOR¹, -NR¹COR¹, -SR¹, NH₂, -N(SO₂R¹)₂,

wherein X^a is halogen, each R¹ is independently H or C₁₋₁₀ alkyl optionally substituted by halogen up to per halo; R^{1a} is C₁₋₁₀ alkyl and p is 0 or 1

and wherein

2 adjacent R^{4'}, R^{5'} and R^{6'} can together with the phenyl form naphthyl, optionally substituted by C₁₋₁₀-alkyl, C₁₋₁₀-alkoxy, C₃₋₁₀-cycloalkyl, C₂₋₁₀-alkenyl, C₁₋₁₀-alkanoyl, and halogen up to perhalo; and

wherein R^{3'} is SO₂F or SO₂CH₂X^a_{3-n}, where n is 0 or 1.